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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,472	02/05/2004	Daniella Licht	29341U	7030

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
09/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,472	LICHT ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29,38-40,42-45,47-76,82-92 and 108-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29,38-40,42-45,47-76,82-92 and 108-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment and remarks dated 5-30-08 is acknowledged.

Claims 1-29, 38-40, 42-45, 47-76, 82-92 and 108-119 are pending in the instant application.

Response to Arguments

1. Applicant's arguments with respect to claims 1-29, 38-40, 42-45, 47-76, 82-92 and 108-119 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1-4, 7-11, 14-20, 29, 38-46, 53-72, 76, 82-89 and 108-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2001/0005512 to Anderson in view of Remingtons' Pharmaceutical Sciences (1990) and US 5994348 ('348) to Ku et al.

OR

Claims 1-4, 7-11, 14-20, 29, 38-40, 42-45, 53-72, 76, 82-89 and 108-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,419,953 to Qiu et al in view of Remingtons' Pharmaceutical Sciences (1990) and US 5994348 ('348) to Ku et al.

Anderson teaches a pharmaceutical composition comprising valproate compounds such as divalproex sodium as an active agent. For the dosage forms containing the active agent, Anderson teaches tablet formulations comprising the active agent and hydroxypropyl cellulose, which read on the instant components i) and ii). For the instant filler, Anderson teaches microcrystalline cellulose and lactose in the above dosage form. For the instant lubricant, Anderson teaches magnesium stearate (paragraphs 0107 – 0114). Anderson also teaches the active agents for the same treatment i.e., epilepsy and bipolar disorder (col. 1-2). Anderson teaches the various tabletting ingredients as percentages of the total weight of the tablet as opposed to the amounts and the tablets of Anderson are prepared in the same manner (compression tablets) as that claimed in the instant i.e., admixing the predetermined amounts and compressing the tablets. Anderson also teaches the excipients for the same purpose i.e., filler, lubricant etc and accordingly, optimizing the amount of an excipient with an expectation to achieve the desired tabletting effect such as lubrication, increasing the bulk (with a filler) etc., would have been within the scope of a skilled artisan.

Qiu et al (Qiu) teaches controlled release composition comprising an anti-epileptic agent, valproic acid or its salts such as an ester, amide etc., prepared by intimately mixing the components of the composition and compression method (lines bridging col. 2-3 & col. 5, L 8-20). The composition, in the form of tablets, contains hydroxypropyl methylcellulose (examples formulations) and excipients such as magnesium stearate, lactose, microcrystalline cellulose (col. 3, L 1-53 & col. 5).

Both Anderson and Qiu fail to teach additional binder and also the specific HPMC with the claimed percentages of HP and MC contents, viscosity, particle sizes etc., in the composition comprising valproic acid or its salts. However, both the references are directed to preparing compressed dosage forms for a controlled release of active agent.

Remingtons' Pharmaceutical Sciences (Remingtons') teach oral dosage forms, particularly, compressed tablets comprising the tabletting excipients such as diluents, binders, disintegrants, glidants etc (pages 134-1637). Remingtons' teach that binders impart cohesiveness to the tablets formulations, which ensures that the tablet remains intact after compression, as well as improving the free-flowing qualities by the formulation of granules of desired hardness and size (page 1635). Among the binders, Remingtons' teach the instant starch, gelatin, sugars; gums, polyethylene glycol, waxes, microcrystalline cellulose, ethylcellulose etc., and in particular teach instant claimed cellulose binders such as hydroxypropyl cellulose or hydroxyethyl cellulose (page 1636, col. 1, last paragraph). Thus, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use a single or more than binder of Remingtons' in the compression tabletting composition of Anderson or Qiu because Remingtons' teach that teach that binders impart cohesiveness to the tablets formulations, which ensures that the tablet remains intact after compression, as well as improving the free-flowing qualities by the formulation of granules of desired hardness and size. Accordingly, depending on the cohesiveness or hardness of the tablet desired, a skilled artisan would have employed an appropriate amount of a binder in the

composition of Anderson or Qiu. Further, with respect to the composition claims reciting specific amounts of fillers, active agent and the disintegrants, absent any unexpected result optimizing the amounts of each of the active agent or the tabletting ingredients (lubricant, filler, disintegrant, release polymer) so as to achieve the desired release rate would have been within the scope of a skilled artisan. For the specific release rates claimed, both Anderson and Qiu recognize the importance of valproic acid in treating the claimed conditions such as epilepsy and also teach the claimed excipients. Accordingly, optimizing the individual amounts of the components of the composition so as to achieve the desired release for an effective treatment with the active agent would have been obvious for a skilled artisan.

Further, Remington's describes that generally disintegrants are mixed with active ingredients and other diluents before granulation. However, it is also stated that sometimes one part of it is added to the powdered formulation before granulation and the remainder mixed with the lubricants and added prior to compression, so as to achieve the raid disintegration as well as rapid dissolution of active agent (col. 2 of page 1637). Remingtons' recognize binders for their ability to disintegrate the tablets by breaking intercrystalline bonds in the disintegration medium (page 1636, col. 1). Therefore, adding the binders, disintegrant and other excipients to valproic acid of Anderson or Qiu either as an extragranulate or an intragranulated (i.e., mixing before granulating or after granulating) would have been within the scope of a skilled artisan because Remington's suggests that depending on the rate of disintegration one can add

the excipients as intragranular or extragranular excipients so as to achieve the desired rate of disintegration and release desired.

While Remington's fail to teach any specific drug and teaches in general tablet preparation, such intragranular and extragranular preparations are routinely prepared in pharmaceutical art in the field of preparing compressed tablets with the desired release rate. This is evidenced by the teachings of Ku ('348), where in col. 5-6, '348 describe the method of preparing by intragranulation and extrangranulation for ease in ejection of tablet after compression and for achieving a specific release or dissolution. Thus, a skilled artisan would have been able to prepare tablet composition of valproic acid in an intragranular or extragranular method depending on the desired dissolution of the tablet.

2. Claims 5-6, 12-13, 21-28, 47-52, 73-75 and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2001/0005512 to Anderson in view of Remingtons' Pharmaceutical Sciences (1990) and US 5994348 ('348) to Ku et al **OR** over US 6,419,953 to Qiu et al in view of Remingtons' Pharmaceutical Sciences (1990) and US 5994348 ('348) to Ku et al as applied to claims 1-4, 7-11, 14-20, 29, 38-46, 53-72, 76, 82-89 and 108-119 above, and further in view of US 4,704, 285 ('285).

Anderson, Qiu and Remingtons', all of the references described above, fail to teach the claimed viscosity of cellulose compounds, % distribution of HP and MC constituents and particle size distribution.

'285 teach compressible tablet preparation with HPMC ether fine particles as a matrix (col. 2, L 7-25). In addition to the active agents and HPMC ether, '285 teach

inclusion of HPMC as a hydrocolloid and suggests that the particle size of HPMC is such that at least 70% pass through 100 mesh, with a HP content of 4%-12% and methoxy content of 19% to 30% (see col. 3, L 37-55). '285 further teach that the viscosity of HPMC is between 100 to 10,000 cps. Thus, the % of the MC and HP contents, viscosity and the particle sizes of instant claims are encompassed by the ranges of prior art. While 285 do not teach the claimed drug, the reference states any drug may be included in the composition. It would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to include HPMC such as that described by 285 in the compressible composition of Anderson or Qiu because all the references are directed to compressible tablets and '285 teach that the claimed HPMC are routinely employed in compressible tablet preparation for improving the flow properties of the tablet and also to achieve sustained release of the active agent from the tablets due to delaying of the release of the active agent by the fine particle nature of the cellulose materials (see lines bridging col. 1-2 of '285). A skilled artisan would have expected to achieve the desired delay in the release of valproic acid or its derivatives of Anderson or Qiu with the incorporation of the cellulose materials of '285 in addition to the excipients taught by Remingtons'.

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Double Patenting

3. Claims 1-29, 38-40, 42-45, 47-76, 82-92 and 108-119 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-55 of copending Application No. 10/772,911 in view of US

4,704,285 ('285), Remingtons' Pharmaceutical Sciences (1990) and US 5994348 ('348) to Ku et al.

Instant claims as well as the co-pending claims are directed to compressible tablets comprising valproic acid or its salts as an active agent, excipients such as HPMC, magnesium stearate, fillers, lubricants etc. Both sets of claims are directed to treating epilepsy, pain and conditions such as bipolar disorder with the above composition. Instant claims differ from the co-pending claims in that instant claims recite HPMC in addition to the binder, whereas the co-pending claims recite hydroxy propyl cellulose and a disintegrant. The co-pending claims fail to claim the specific viscosity or the percentages of the methoxy or hydroxy propyl content of HPMC. Further, instant claims release sustained and the copending claims have been amended to recite immediate release.

'285 teach compressible tablet preparation with HPMC ether fine particles as a matrix (col. 2, L 7-25). In addition to the active agents and HPMC ether, '285 teach inclusion of HPMC as a hydrocolloid and suggests that the particle size of HPMC is such that at least 70% pass through 100 mesh, with a HP content of 4%-12% and methoxy content of 19% to 30% (see col. 3, L 37-55). Thus, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to include HPMC such as that described by 285 in the compressible composition of instant claims because all the references are directed to compressible tablets and '285 teach that the claimed HPMC are routinely employed in compressible tablet preparation for improving the flow properties of the tablet. '285 further teach that the viscosity of HPMC

is between 100 to 10,000 cps. Thus, the % of the MC and HP contents, viscosity and the particle sizes of instant claims are encompassed by the ranges of prior art. With respect to the claimed release rates, both sets of claims are directed to the same method of treatment with the same active compound and accordingly, optimizing the individual amounts of the components of the composition so as to achieve the desired release for an effective treatment with the active agent would have been obvious for a skilled artisan. With respect to the extragranular limitation, the teachings of Remingtons' and '348 have been discussed above and accordingly, a skilled artisan would have been able to prepare a tablet composition of valproic acid in an intragranular or extragranular method depending on the desired dissolution of the tablet and the release of the active agent.

This is a provisional obviousness-type double patenting rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner,
Art Unit 1611
September 1, 2008